



Identification of promoters and enhancers induced by carbon nanotube exposure

Bornholdt, Jette; Lilje, Berit; Saber, Anne Thoustrup; Boyd, Mette; Jørgensen, Mette; Chen, Yun; Vitezic, Morana; Jacobsen, Nicklas Raun; Poulsen, Sarah Søs; Andersson, Robin

Total number of authors:

16

Publication date:

2015

Document Version

Publisher's PDF, also known as Version of record

[Link back to DTU Orbit](#)

Citation (APA):

Bornholdt, J., Lilje, B., Saber, A. T., Boyd, M., Jørgensen, M., Chen, Y., Vitezic, M., Jacobsen, N. R., Poulsen, S. S., Andersson, R., Hougaard, K. S., Yauk, C. L., Halappanavar, S., Wallin, H., Vogel, U. B., & Sandelin, A. (2015). *Identification of promoters and enhancers induced by carbon nanotube exposure*. Abstract from First Annual Danish Bioinformatics Conference, Odense, Denmark.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

21 Optimization of flanking region lengths for folding into constrained RNA structures: RNAcop.

Nikolai Hecker, Mikkel Christensen-Dalsgaard, Stefan E. Seemann, Jakob H. Havgaard, Peter F. Stadler, Ivo L. Hofacker, Henrik Nielsen, Jan Gorodkin.

Center for non-coding RNA in Technology and Health and Department of Veterinary Clinical and Animal Science and Department of Cellular and Molecular, Medicine, University of Copenhagen, Denmark; Bioinformatics Group, Department of Computer Science & IZBI-Interdisciplinary Center for Bioinformatics & LIFE-Leipzig Research Center for Civilization Diseases, University of Leipzig, Germany; Department of Theoretical Chemistry, University of Vienna, Austria.

RNA secondary structure prediction is often performed with the aim to identify functional elements. Especially for screens for structured non-coding RNAs or predicted structures in untranslated regions of a mRNAs, the length of such an element is not well defined. For in vitro experiments, however, a smaller part of an entire transcript comprising the predicted structure is usually extracted. Here, the composition of flanking nucleotides can disturb folding into the structure of interest.

Therefore, we developed a computational tool, RNAcop (RNA context optimization by probability), that optimizes folding into the structure of interest. Using constrained folding, our approach computes probabilities for folding into the structure of interest for all pair-wise combinations of flanking region lengths. Our analysis suggests that proper choices of flanking regions are crucial for a number of structures. The results are supported by in vitro experiments. RNAcop is available as web server and command-line tool at <http://rth.dk/resources/rnacop>.

22 Identification of promoters and enhancers induced by carbon nanotube exposure .

Jette Bornholdt, Berit Lilje, Anne Thoustrup Saber, Mette Boyd, Mette Jørgensen, Yun Chen, Morana Vitezic, Nicklas Raun Jacobsen, Sarah Søs Poulsen, Robin Andersson, Karin Sørig Hougaard, Carole L Yauk, Sabina Halappanavar, Håkan Wallin, Ulla Vogel, Albin Sandelin.

The Bioinformatics Centre, Department of Biology & Biotech Research and Innovation Centre, University of Copenhagen, Denmark; National Research Centre for the Working Environment, Copenhagen, Denmark; Environmental and Radiation Health Science Directorate, Ontario, Canada; Institute of Public Health, University of Copenhagen, Denmark; Department of Micro and Nanotechnology, Technical University of Denmark.

Usage of carbon nanotubes (CNTs) is increasing in industry due to their mechanical and electrical properties. However, pulmonary exposure to CNTs induces, an asbestos-like toxicological response characterized by persistent inflammation, granuloma formation and fibrosis with low no-effect levels. Little is known about the regulation of the response to CNTs. To this end, we have profiled transcription start sites and enhancers in mouse lung tissues following CNT exposure using Cap Analysis Gene Expression Assay (CAGE). This revealed a massive transcriptome response, with over 100-fold expression increases for key promoters, and a large change in transcription of enhancer regions linked to similarly responding genes. The response included key genes involved in inflammation, phagocytosis, cell and proliferation. We found a clear correlation between the overall CNT response strength and the number of alternative promoters in a given gene, but not the number of proximal enhancers. Upregulated genes after CNT exposure, where only the most annotated upstream promoter was upregulated, were associated to inflammation. Also NFkB binding sites were over-represented among these promoters. Conversely, upregulated genes where the upregulation could be attributed to promoters within the gene were not in particular linked to inflammation, and these promoters had distinct DNA motif enrichment patterns, not including the NFkB binding sites. Interestingly, NFkB binding sites were not over-represented in upregulated enhancer regions.